Shoulder and neck pain during office work

The significance of muscle activity and microcirculation

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Oslo, July 2009

Vegard Strøm

Abbreviations

ACR	American College of Rheumatology
ANOVA	analysis of variance
ATP	adenosine trisphosphate
BP	blood pressure
Ca	calcium
CI	confidence interval
CNS	central nervous system
C7	the 7th cervical vertebrae of the spine
EMG	electromyography
5-HT	5-hydroxytryptamine or serotonin
HR	heart rate
kPa	kiloPascal
LDF	single-fiber laserDoppler Flowmetry
MAP	mean arterial blood pressure
min	minute
mm	millimeter
ms	millisecond
MSI	musculoskeletal complaint severity index
MVC	maximal voluntary contraction
NIRS	near-infrared spectroscopy
PPT	pressure pain threshold
rms	root mean square
sec	second
SD	standard deviation
SE	standard error of the mean
TM	trapezius myalgia
VAS	visual analogue scale

List of papers

Paper I

Strøm V, Knardahl S, Stanghelle JK, Røe C. Pain induced by a single simulated office-work session: Time course and association with muscle blood flux and muscle activity. Eur J Pain, 2008. doi:10.1016/j.ejpain.2008.11.003.

Paper II

Strøm V, Røe C, Knardahl S. Work-induced pain, trapezius blood flux, and muscle activity in workers with chronic shoulder and neck pain. Pain, 2009;144:147-155.

Paper III

Strøm V, Røe C, Matre D, Knardahl S. Pressure pain thresholds and salivary cortisol in response to simulated office work in subjects with and without chronic shoulder and neck pain. Submitted.

Paper IV

Strøm V, Røe C, Knardahl S. Coffee intake and development of pain during office work. Submitted.

Summary in English

Pain in the neck and shoulder region is common in office work involving very low-level muscle activities. The pathogenetic mechanisms underlying the pain development are poorly understood. Evidence for an association between muscle activity and pain is conflicting. Hypotheses focusing on factors regulating blood vessels and/or factors from the microcirculation that activate nociceptors have been proposed.

The overall objective of this thesis was to elucidate the significance of muscle activity and microcirculation in shoulder muscles as possible mechanisms underlying development of pain in the shoulders and neck during office work.

We established in the laboratory a computer-based work task which models office work (work processing). The task comprised a 90 min work without pauses, and with high hand precision demands and time pressure. Twenty-four subjects, 14 women and 10 men, with chronic shoulder and neck pain, and 28 healthy pain-free reference subjects, 16 women and 12 men, were recruited. The measurements included ratings of pain intensity, intramuscular trapezius blood flux by laser-Doppler flowmetry (LDF), trapezius muscle activity by surface electromyography (EMG), pressure pain thresholds (PPT), and salivary cortisol.

The subjects, both with and without shoulder and neck pain, developed substantial pain during the work task, but with different time courses. The level of muscle activity was very low during the task (< 4% of EMG during maximal voluntary contraction; MVC). The LDF revealed local vasodilation throughout the work task in both groups. Shoulder PPT decreased from pre- to post-task similarly in both groups. Salivary cortisol levels remained stable during the work task. We found no correlations between pain and muscle activity. There were positive correlations with pain and blood flux in the pain-afflicted subjects and negative correlations in the reference group. For both groups this correlation was stronger after 30-45 min of the time spent on the work task.

The findings from the present studies suggest that office work involving time pressure and precise hand movements may induce substantial shoulder and neck pain and deep tissue hyperalgesia both in healthy pain-free subjects and in people

with chronic shoulder and neck pain. This pain development seems to be related to the microcirculation of the upper trapezius muscles and not to the muscle activity.

Norsk sammendrag

Smerter i nakke og skulderregionen er vanlig hos personer som utfører kontorarbeid til tross for at slikt arbeid involverer veldig lavt muskelaktiveringsnivå. De patogenetiske mekanismene som ligger til grunn for slik smerteutvikling er imidlertid ikke fullt ut klarlagt. Evidens for en sammenheng mellom muskelaktivering og smerteutvikling synes å være motstridene. Derfor er det fremsatt hypoteser som hevder at muskelsmerter kan skyldes samspill mellom regulering av mikrosirkulasjon og aktivering av nociseptorer.

Hovedhensikten med dette doktorgradsarbeidet har vært å belyse betydningen av muskelaktivering og lokal blodsirkulasjon i skuldermuskulaturen som mulige mekanismer til grunn for utvikling av muskelsmerter i nakke og skulder ved kontorarbeid.

Vi har i vårt laboratorium etablert en PC-basert kontorarbeidsoppgave, utformet som et tekstrettingsarbeid som gjennomføres i løpet av 90 min uten pause og med tidspress og høye krav til presisjon. Tjuefire personer med kroniske nakke-/skuldersmerter (14 kvinner og 10 menn; smertegruppe) og 28 friske, smertefrie personer (16 kvinner og 12 menn; referansegruppe) ble inkludert i studien. Underveis i arbeidsoppgaven ble smerteintensitet rapportert på visuell analog skala (VAS), mikrosirkulasjon og muskelaktivering i øvre del av skuldermuskulaturen (trapezius) ble målt ved bruk av henholdsvis intramuskulær laser-Doppler flowmetry (LDF) og overflate-elektromyografi (EMG). I tillegg ble det målt trykksmerteterskel i skuldrene og kortisolnivå i spytt.

Resultatene viste at personer både med og uten kroniske nakke-/skuldersmerter utviklet betydelig smerter underveis i arbeidsoppgaven, men tidsforløpet var ulikt; Personene i smertegruppen fikk en betydelig smerteøkning i starten av arbeidet, mens personene i referansegruppen fikk en betydelig økning i smerteintensitet mot slutten av arbeidet. Muskelaktiveringen i trapezius var lav (< 4% av EMG målt under maksimal voluntær muskelkontraksjon, MVC) gjennom hele arbeidsperioden hos begge grupper. Blodsirkulasjonen lokalt i øvre trapezius økte betydelig ved oppstart av arbeidet hos personer i begge grupper og fortsatte å øke inntil en fallende tendens startet etter ca ½ times arbeid. Etter avsluttet arbeid ble blodsirkulasjonen redusert til utgangsnivå i referansegruppen, men ikke i

smertegruppen. Trykksmerteterskelen i skuldrene var hos begge grupper redusert etter arbeidet sammenliknet med før start. Nivået av kortisol endret seg ikke under arbeidet. Vi fant ingen signifikante korrelasjoner mellom smerte og muskelaktivering. Derimot fant vi positive korrelasjoner mellom smerte og blodsirkulasjon i smertegruppen og negative korrelasjoner hos de friske. Denne sammenhengen var sterkest mot slutten av arbeidet hos begge gruppene.

Funnene i denne avhandlingen antyder at kontorarbeid med PC under tidspress og med høye presisjonskrav kan føre til betydelige smerter i nakke og skulder både hos friske, smertefrie personer og personer med kroniske nakke- og skuldersmerter. Smerteutviklingen i nakke og skulder synes å være relatert til blodsirkulasjonen lokalt i trapezius, mens muskelaktiveringen ikke synes å være av betydning.

1. Introduction

Musculoskeletal disorders are a common health problem afflicting a substantial proportion of the adult population and affecting negatively several aspects of quality of life.

Musculoskeletal disorders in the upper extremities refers to injuries affecting the soft tissues of the neck, shoulder, elbow, hand, wrist, and fingers (Tittiranonda et al., 1999) and include pain conditions that involve the nerves, tendons, muscles, and supporting structures of the body (Bernard et al., 1997). Musculoskeletal disorders are the most common cause of sick leave in Norway. In 2008 it accounted for 33.5% of all sick leave cases, of which approximately 8% was ascribed to disorders in the neck, shoulders, and arms (NAV, 2009).

In the general Norwegian population the prevalence of chronic pain is reported to be between 24% and 30% (Rustøen et al., 2004;Breivik et al., 2006). Of those that in the study by Rustøen et al. (2004) reported to have chronic pain (i.e. of >3 months duration), 65% indicated that the pain had lasted more than five years and in 57% the cause of the pain was unspecified.

In the working population work-related musculoskeletal pain in the neck and shoulder region exhibit prevalence rates of 30% or higher (Buckle and Devereux, 2002;Punnett and Wegman, 2004). Twenty-three per cent of European workers report having muscular complaints (Safety and Health at Work,EU, 2007). Prolonged neck and shoulder symptoms influences work productivity (Hagberg et al., 2002;van den Heuvel et al., 2007). In a survey among 28 000 workers in the US lost productivity due to common pain conditions was estimated to cost more than US $61 billion per year, and seemed mainly to be attributed to reduced performance at work, not to being absent from work (Stewart et al., 2003).

Thus, musculoskeletal pain disorders represent an enormous demand on society, where the costs of sick leave adds to the cost of lost productivity making this a considerable economic challenge in addition to the personal distress involved.

1.1 Office work

Heavy physical workload increases the risk of musculoskeletal disorders (Karpansalo et al., 2002;Hamberg-van Reenen et al., 2006). However, the nature of the working life has changed during the last decades. The number of people doing heavy manual work has been reduced. An increasing number of people work with computers. In 2007 about 30% of all employees in EU reported using computers all or most of the time for their work (Safety and Health at Work, EU, 2007).

Work at computers may represent interactions among various work dimensions as ergonomic, work organizational, psychological, and social stressors (Punnett and Bergqvist, 1997). The physical exposure on the shoulders and neck during work with a computer or other office work is very low. Most studies report muscle activity levels below ten percent of EMG_{max} (Westgaard et al., 2001;Røe and Knardahl, 2002;Wahlstrom et al., 2003; Blangsted et al., 2004). Shoulder and neck pain is common during work involving very low levels of muscle activity, as during repetitive industrial work (Andersen et al., 2002;Leclerc et al., 2004) and during office work with computers, where prevalence rates of up to10% have been reported (Gerr et al., 2002; Brandt et al., 2004). Computer use has been found to be a risk factor for developing musculoskeletal symptoms in upper extremities (Jensen et al., 1998;Punnett and Bergqvist, 1999). Physical exposures during office work that may increase the risk of such symptoms include continuous work, repetitive tasks (Punnett and Bergqvist. 1997), static muscular activation (Jensen et al., 1998), visual strain (Woods, 2005), long duration of computer use, awkward positions (Tittiranonda et al., 1999), and the amount of computer mouse usage (Andersen et al., 2008). Mental demands like high quantitative job demands (e.g. time pressure and precision demands), low control of the work situation, low social support, and low job satisfaction are also found to be risk factors for developing musculoskeletal symptoms in the upper extremities (Ariens et al., 2001;Laursen et al., 2002;Hannan et al., 2005).

1.2 Muscle pain

Pain can be defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such

damage" (International Association for the Study of Pain, IASP, 1979). Hence, pain is a subjective experience.

Muscle pain, originating in striated muscle including its fascia and tendinous insertions, differs from cutaneous pain in that it is perceived as aching and cramping and is often difficult to localize (Mense, 2003), while cutaneous pain is localized and characterized as sharp, pricking, stabbing or burning (Mense, 1993). In order to elicit muscle pain, small-diameter afferent sensory fibers from muscles have to be activated via free nerve endings – *nociceptors* (Millan, 1999).

In the skeletal muscles nociceptors are located at the wall of arterioles and the surrounding connective tissue (Mense, 1993). Nociceptors are specialized noxious stimulus detectors (Woolf and Ma, 2007), and normally only activated by noxious (i.e. tissue threatening) or potentially noxious stimuli (Mense, 1993). The nociceptors in muscles are connected with the central nervous system (CNS) by rapid conducting thin myelinated (A-δ fibers or group III) or slowly conducting unmyelinated (C-fibers or group IV) nerve fibers (Mense, 2003). The cell bodies of nociceptors are located in the dorsal root ganglion or trigeminal ganglia and give rise to a single axon that divides into a peripheral branch that innervates peripheral target tissue (peripheral terminal), and a central axon that enters the CNS to synapse on nociceptive second order neurons (Woolf and Ma, 2007), that in turn project axons and transmit pain messages to higher brain centers, including thalamus and cerebral cortex (Julius and Basbaum, 2001).

Nociceptors have characteristic thresholds or sensitivities that distinguish them from other sensory nerve fibers (Julius and Basbaum, 2001). A decrease in threshold or an augmented response to suprathreshold stimuli, i.e. *sensitization*, can be defined as "a leftward shift of the stimulus-response function that relates magnitude of the neural response to stimulus intensity" (McMahon and Koltzenburg, 2006). When synaptic responses of the nociceptors are progressively amplified pain is the result (Woolf and Ma, 2007). Sensitization can occur both at peripheral sites and at the spinal and medullar level (Mense, 2003). Peripheral sensitization is a form of stimulus-evoked functional plasticity of the nociceptors (Woolf and Ma, 2007). The stimulus can be a set of inflammatory mediators, collectively referred to as the "inflammatory soup" (Mense, 2009), released from injured and inflammatory cells that sensitize the nociceptors, reducing threshold and increasing responsiveness

(Woolf and Ma, 2007). As a result of the change in the chemical milieu, nociceptors change from being detectors only of noxious stimulus to be detectors also of innocuous input, and low-intensity stimulus therefore starts producing pain (Woolf and Ma, 2007). The increased sensitivity normally is restricted to the site of inflammation (Ji et al., 2003). The components of the "inflammatory soup" include bradykinin, prostaglandins, serotonin (5-HT), ATP, nerve growth factor, interleukins, and glutamate (Julius and Basbaum, 2001;Woolf and Ma, 2007;Mense, 2009), as well as adenosine (Sawynok and Liu, 2003). Central sensitization refers to an increased excitability (reductions in threshold and increased responsiveness) of nociceptive neurons in the dorsal horn of the spinal cord and is normally initiated only by nociceptor sensory inflow (Ji et al., 2003). Central sensitization has been suggested to be a primary explanation for the transition from acute to chronic muscle pain (Mense, 2003;Larsson et al., 2007).

1.3 Possible pathogenetic mechanisms

In order to optimize prevention and treatment of musculoskeletal disorders, better understanding of the pathogenetic mechanisms involved in development of these disorders would be crucial. Several hypotheses have been proposed in order to explain the pathophysiological mechanisms involved in the development of muscle pain.

Since Travell and coworkers (1942) proposed that 'the pain is a consequence of a sustained spasm of skeletal musculature', conventional wisdom has assumed that muscle pain stems from muscle fiber activity leading to an energy crisis. Their theory, *the hyperactivity hypothesis*, was one of the first models to suggest a causal relationship between muscle activity and pain. It was primarily based on observation of muscle stiffness and decreased relaxation ability, implying the existence of a positive feedback loop of muscle spasm causing muscle pain, leading in to a vicious circle.

Later on, the *vicious circle hypothesis* was proposed, by Schmidt et al. (1981), and refined by Johansson and Sojka (1991) and Johansson et al. (1999). They suggested that the γ-muscle spindle system plays a central role in a self-maintaining vicious-circle in which pain and muscle activity amplifies each other. This hypothesis

assumes that during muscle contractions metabolites activates chemosensitive nociceptive types III and IV muscle afferents, which in turn activate the γ-motor neurons. Elevated γ-motor neuron activity causes elevated muscle spindle activity, which in turn increases muscle fiber contraction, increase stiffness and then increase the production of metabolites, thus a vicious circle. This hypothesis does not seem to explain the initiation of pain, but merely give an explanation for the sustainment of muscle pain.

Based on a literature review on motor function in five chronic musculoskeletal pain conditions and the findings from their own experimental tests, Lund et al. (1991) proposed *the pain-adaptation model*. This model was based on the finding of reduced activity, not hyperactivity as in the vicious circle model, in agonist muscles by pain, leading to reduced force production and movement velocity. The hypothesis proposes that decreased motoneuron output to agonists and increased activity to antagonist act as a protective reflex adaptation to pain. The dysfunction seen in several types of chronic musculoskeletal pain is thus suggested to be a normal protective adaptation to avoid the muscle from further damage rather than the cause of pain (Lund et al., 1991). Hence, the origin of pain has to come from other muscle factors or from other components of the motor systems (Knardahl, 2002).

During work with sustained high static loads, ischemia and hypoxia leading to energy crisis of muscles or tendons are plausible mechanisms to explain the pain (Hagberg, 1984;Jensen et al.,1995a;Palmerud et al., 2000;Sjogaard et al., 2004). Ischemia occurs when the intramuscular pressure exceeds the perfusion pressure of the microcirculation, and thereby impedes the blood flow (Blair et al., 2003).

The fact that myalgia can occur even at very low levels of contractions when the circulation seems adequate led to proposal of the *Cinderella-fiber hypothesis* (Hägg, 1991). According to Henneman's size principle the small type I motor units are recruited first during any contractions. These fibers remain continuously activated during the period of muscle activity (Henneman et al., 1965). These units would then have a high activity level, even when the activity of the muscle as a whole is low. The hypothesis suggests that these low threshold motor units are overloaded during sustained occupational static work, leading to metabolic changes and energy crises. However, derecruitment and substitutions of motor units takes place (e.g. Visser and van Dieën, 2006).

A development of the Cinderella hypothesis is the suggestion that calcium (Ca^{2+}) plays a central role in the development of muscle pain during prolonged low-level muscle activity, as proposed by Gissel (2000). Sustained motor unit activity results in intracellular accumulation of Ca^{2+}, which might have noxious effects on the membranes of the muscle fibers (Gissel, 2000). This hypothesis maintains that membrane leakage is likely to result in pain sensation in the damage muscle (Gissel, 2000).

All the explanatory models of pathophysiological mechanisms considered above, except the pain-adaptation model, assume that muscle-cell activity during work with low-level muscle activation produce pain. Since these metabolic effect hypotheses seem to fail in explaining how low-level muscle activation is translated into activation of nociceptor nerves, Knardahl (2002; 2005) proposed that factors regulating blood vessels and/or factors from the microcirculation activate nociceptors – *the blood vessel-nociceptor interaction hypothesis*. In the skeletal muscles nociceptors are located at the wall of arterioles and in the surrounding connective tissue (Mense, 1993). This hypothesis proposes that muscle pain arises from interaction between vessel and nerve of the connective tissue of the muscle, thus assuming muscle cell activity not to be the primary cause of the pain. Putative mechanisms of muscle pain proposed by this hypothesis are vasodilation, vascular production and release of algogenic factors, and inflammation (Knardahl;2002;2005). The lack of pain during post-exercise vasodilation indicates that vasodilation alone, by stretching the blood vessel wall and the adjoining tissue and then producing mechanical activation of nerve endings, is not sufficient to produce pain. Both the nerves that innervate the blood vessels and the vessels themselves may produce factors that contribute to nociception, like prostaglandins, bradykinin, nitric oxide, and serotonin. Release of inflammatory mediators, including histamine and substance P, and leakage of cells and algogenic factors from the plasma space may activate or sensitize nociceptors. This hypothesis has yet to be verified in experimental studies. To test this hypothesis studies of the muscle microcirculation are needed, in which the present thesis are dealing with.

Likely, the pathogenesis of work-related shoulder and neck pain is of multifactorial origin. The contribution of pathogenic factors are likely to vary between different exposures, between different contraction types (i.e. static or

dynamic), between different contraction intensities (i.e. high- and low force activities), and between individuals.

1.4 Study objectives

The overall objective of this thesis was to elucidate the significance of muscle activity and microcirculation as possible mechanisms underlying development of musculoskeletal pain in the shoulders and neck during office work.

The specific aims of this thesis were to:

1. Determine if office work with time pressure and high hand precision demands elicits pain (Paper I and II).
2. Determine if pain provoking office work alters muscle activity in the upper m. trapezius (Paper I and II).
3. Determine if pain provoking office work alters local muscle blood flow in the upper m. trapezius (Paper I and II).
4. Determine if pain provoking office work induces changes in pressure pain thresholds (Paper III).
5. Determine if subjects with chronic shoulder and neck pain respond differently to pain provoking office work than healthy pain-free subjects in pain, blood flow, muscle activity (Paper II), and in pressure pain thresholds (Paper III).
6. Determine if shoulder and neck pain is related to the muscle activity in the m. trapezius (Paper I and II).
7. Determine if shoulder and neck pain is related to the microcirculation in the m. trapezius (Paper I and II).
8. Determine if subjects who had consumed coffee before starting a pain provoking office work task exhibited different time course in the pain development and intramuscular trapezius blood flux than the subjects who had abstained from coffee intake (Paper IV).

2 Methods

Subjects

Pain-afflicted subjects: Twenty-four subjects, 14 women and 10 men, with chronic shoulder and neck pain (pain group), were recruited through advertisements in local papers and the Internet. Three of the subjects (two women) reported having had shoulder and neck pain for less than 12 months, 13 (7 women) for 1–4 years, three (all men) for 5–10 years, and five (all women) for more than 10 years.

Inclusion criteria were: Pain in the shoulders or neck for at least 2–3 days per week during the previous 4 weeks, tender points in the corresponding muscle, age between 18 and 45 years, and working more than 80% fulltime and working with a computer more than 20% of the working time. The subjects also had to be familiar with the Norwegian language in order to perform the text-editing task.

Exclusion criteria were: cervicobrachialgia; rotator tendinosis or other shoulder disorders; inflammatory, metabolic or cardiac diseases; regular medication of importance for circulation; pregnancy; alcohol or medicament abuse; or dyslexia.

Pain-free subjects: A group of 28 healthy pain-free subjects, 16 women and 12 men, comprised a reference group. They were recruited with the same inclusion and exclusion criteria, except that subjects with current musculoskeletal pain were excluded.

In Paper I only the subjects in the reference group were included. Paper II-IV included the subjects from both the pain and reference groups.

Ethics

All participants received written information and signed an informed consent form. The Norwegian Regional Committee for Medical Research Ethics and the Norwegian Social Science Data Services approved the study.

Medical examination

A standardized clinical examination was performed by a specialist in physical medicine and rehabilitation, and included range of motion of the cervical spine and shoulders, tests for nerve compression in the neck and upper extremities, and tests

for subacromial problems. A neurological examination of muscle force, reflexes, and sensory function was performed on the upper extremities to identify any exclusion criteria. Tender and trigger points in the neck and shoulder muscles, and the typical areas of tenderness in fibromyalgia, were examined. None of the subjects fulfilled the ACR criteria for fibromyalgia (Wolfe et al., 1990), but all subjects in the pain group had tender points in the upper trapezius muscles (i.e. perceived pain on testing). Of totally 18 trigger points tested, a response was found in a median of 5 points (range 2–16; no sex difference, $p = 0.3$).

2.1 Study design

All investigations of this thesis took place in a laboratory setting. We designed the study in order to mimic real office-work activities as text editing. Previous laboratory studies have used computer work tasks like the Stroop Color Word Test or a complex two choice reaction-time task that according to Wahlström et al. (2002) are not easily transferred to real work situations.

The devised office-work model (i.e. the computer-based office-work task) used, was the same in all papers included. An overview of the study design and the different measurements used is given in Fig. 1.

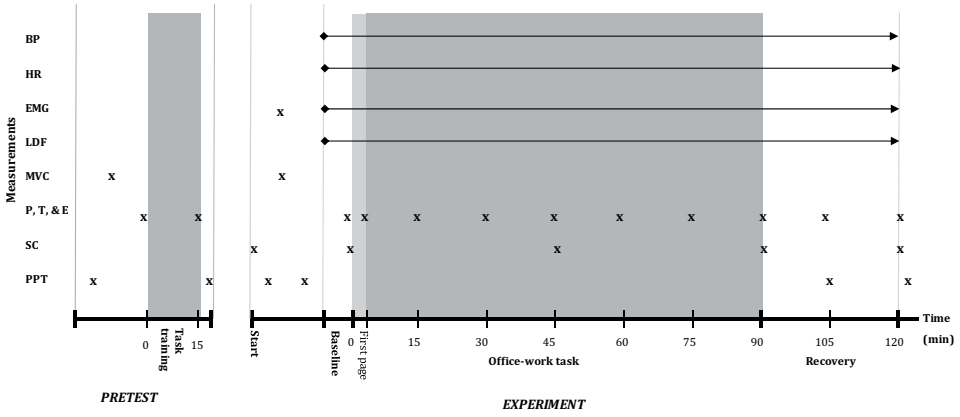

Fig. 1. Schematic overview of the study design. The subjects reported to the laboratory twice. On average, 6 days (range 1–12 days) separated the two sessions. During the first session (pretest) the subjects underwent a standardized medical examination and they were familiarized with the measurements and the procedures for the computer office-work task session (experiment), including a 15 min training session for the word processing task, in which they were encouraged to work as fast and accurately as possible without any pauses. The horizontal axes show the time (min) with the different measurements listed on the vertical axis. Thin solid horizontal arrow lines indicate the time period for continuously data sampling and the **x**'s indicate the time points for non-continuously data sampling. The shaded areas indicate the computer office-work task periods. Duration of baseline was three minutes and the mean time to complete the 1. page during the work task was 1 min 40 sec. BP; mean arterial blood pressure, HR; heart rate, EMG; electromyography, LDF; laser-Doppler flowmetry, MVC; maximal voluntary contraction, PPT; pressure pain threshold, P,T,& E; pain, general tension, and eyestrain, SC; salivary cortisol.

Time-control session

In order to check if the responses found during the experimental session was due to the imposed work task demands a time-control session was carried out with very low work demands (presented in this section only and not in Papers I-IV).

Recruitment of healthy pain-free subjects was done with the same inclusion criteria as described above. The procedure was the same as for the experimental session. Two weeks after the experimental session they repeated the complete experiment, except that the office work task was performed with very low work demands (i.e. no time pressure and no precision demands). The order of the sessions was not randomized in order to ensure the same procedure as for those subjects already included. The work task of the time-control session was to read, in a self-determined pace, the text on the screen, and the subjects were told that they had to

answer a few questions addressing the content of the text after the test. Only two errors were to be corrected at each page with no precision demands imposed since the errors were long words repeated in the text, and no reward was to be obtained.

Only four subjects (two women) were willing to participate in the time-control session, thus due to too few subjects carrying out this session statistical comparisons with the results from the experimental session were not done. The results from the experimental session for these four subjects are, however, included in the papers presented. It became apparent that the subjects were unable to sit still without moving in their chair during the control session and thus exhibited many more movements throughout this session. The results revealed only a minor pain and general tension during the work task (Fig. 2a). The eye strain, however, showed the same time pattern as in the experimental test, but at a considerable lower level. The EMG level in the upper trapezius was below 1 %EMG_{max} except for a transient increase in the active side during completion of the first page (Fig. 2b). The muscle activation in the active m. extensor digitorum was stable throughout the work at about 4 %EMG_{max}. The blood fluxes in both sides of the upper trapezius exhibited a linear and similar increase throughout the work session (Fig. 2b).

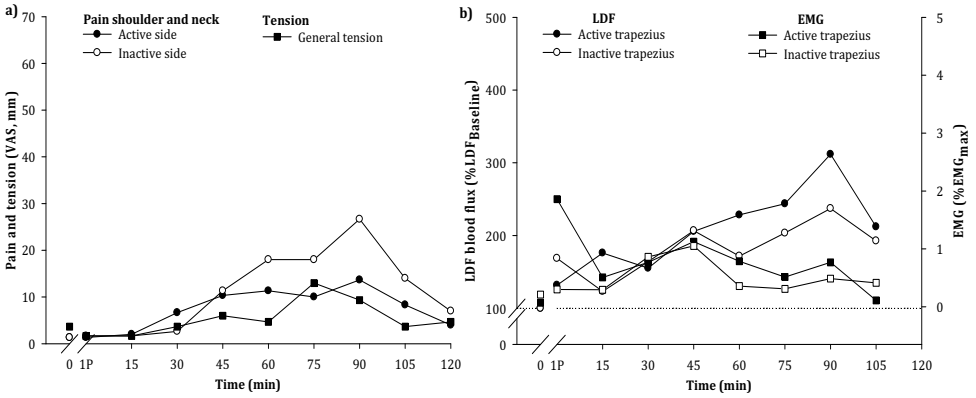

Fig. 2. Control session. Mean values of a) ratings at visual analogue scale (VAS) of pain intensity in the shoulders and neck, and general tension, and b) intramuscular laser-Doppler flowmetry (LDF) blood flux, and surface electromyography (EMG) in the upper trapezius muscle, at baseline (0), after completion of the first page of the work task (1P), and during each 15 min period of the 90 min work task and 30 min recovery. LDF and EMG data are omitted during the last 15 min of the recovery due to major movement artifacts.

2.1.1 Experimental protocol

At the experimental day each subject reported to the laboratory between 8 and 9 a.m. All subjects had ingested a light breakfast of their own choice (not standardized), on average 1 h and 20 min before attending the laboratory. Nine of the subjects in the pain group (six women) and 11 in the reference group (eight women) had consumed one cup of coffee or tea with breakfast. None performed exhaustive physical activity during the 24 h before the experiment.

At the experimental startup, saliva for cortisol measurements were collected and pressure pain thresholds (PPT) determined. Surface electromyography (EMG) electrodes were applied (see 2.2.2), and the subject performed a maximal voluntary contraction (MVC) of shoulder abduction and wrist extension. The laser-Doppler probes to measure blood flux in the trapezius were inserted (see 2.2.3), and a finger cuff to measure blood pressure (MAP) and heart rate (HR) was applied.

The computer task was explained carefully, and the participant adjusted the chair height and the distance to the computer screen to ensure comfortable seating, with the arms resting at the computer table (Fig. 3). The subject was asked to avoid unnecessary movements and talking during the work task. The task started with 3 min of baseline measurements, during which the subject was asked to close the eyes and sit as still and relaxed as possible, after which he or she rated the pain intensity, tension, and eyestrain on the visual analogue scale (VAS), and saliva for cortisol measurements was sampled. The subject gave another VAS rating immediately after finishing the first page of the word processing task and every 15 min thereafter during the 90 min computer work task and the 30 min recovery. Saliva samplings were repeated at 45 min and 90 min of the work task and after 30 min of recovery. Post-PPT measurements were performed 15 min and 30 min into the recovery period.

2.1.2 Computer-based office-work task

The computer-based office-work task consisted of correcting typographical errors in a standardized text using a word processor as fast and as accurately as possible for 90 min. There were no pauses, and the reporting of pain and tension on

the VAS was incorporated into the task using the same hand operations. The text was presented on a 17-inch LCD monitor, and each page comprised about 200 words with 20 spelling errors per page. The subject used the mouse only; first to mark the letter to be removed and then pointed and clicked at the delete symbol. In order to reduce the cognitive workload of the task the words with spelling errors were underlined in red, making them easy to locate. When a correction was made, the underlining disappeared. The participants used the dominant hand on the computer mouse and left button.

Fig. 3. Experimental set-up. The computer office work-station is seen to the right and the investigators control-station to the left.

Precision demands, time pressure, and performance

The task was designed to pose a high demand for hand precision in that all errors to be corrected required marking the letters f, i, j, l, and t in the letter type Arial in 11-point font.

To induce time pressure an individual performance target was set for each subject. The shortest time spent to complete one page correctly was recorded during the pretest session. Using this time per page, the number of pages to complete for each 15 min was calculated, and this served as the individual criterion for attaining a monetary reward, NOK 25 each 15 min period, giving a total obtainable reward of

NOK 150. If any errors remained after a 15 min period, no reward was obtained in that period. Before starting the work task, each subject was told how many pages he or she had to complete during each 15 min period to attain the reward. During the task, the subject received no information about the performance from the investigator but was told to keep pace by oneself.

The mean target for subjects in the pain group was 10 ± 2 (SD) pages vs. 11 ± 2 pages in the reference group (p = 0.08), corresponding to a mean working pace of 90 ± 19 sec and 82 ± 15 sec per page, respectively. The target for the healthy men was higher than that of the healthy women (12 ± 3 pages vs. 10 ± 2 pages, p = 0.04). It was no target difference between men and women in the pain group (p > 0.6).

During the 15 min work task training at the pretest the subjects of the pain group correctly completed 6.5 ± 1.9 pages vs. 7.3 ± 1.8 pages in the reference group (p = 0.12)

During the 90 min work task the subjects in the reference group completed correctly more pages in total than that in the pain group, 58 ± 11 pages vs. 52 ± 12 pages, p = 0.05. The men in the reference group completed correctly more pages in total than the women (63 ± 12 pages vs. 54 ± 9 pages, p = 0.04), while no significant difference was found between the men and women in the pain group (53 ± 9 pages for the men vs. 51 ± 14 for the women, p = 0.8). The number of pages in short of the target accumulated during all the six 15 min periods was similar in the groups (p = 0.82), as well as the obtained amount of reward (NOK 81 ± 41 in the pain group vs. NOK 77 ± 36 in the reference group (p = 0.8).

2.2 Measurements

2.2.1 Pain, general tension, and eyestrain

Subjective reports of the current pain intensity in the right and left shoulder and neck and right and left forearm and wrist, general tension, and visual strain, were reported on VASs comprising 100 mm lines anchored by the labels “no pain/no tension/strain” (0) and “intolerable pain/maximal tension/strain” (100). All ratings, from baseline and throughout the work task and recovery, were entered on the computer screen using the computer mouse to copy and paste a marker into the 100 mm line. The subjects were told to make the ratings as fast and accurately as possible

to avoid unintended pauses, and they were not allowed to see previous ratings. Hence, both the work task and the subjective reporting were performed with the same hand operations and without significant pauses.

2.2.2 Force and electromyography

Individual maximal muscle activation (EMG_{max}) in the upper trapezius and extensor digitorum communis muscles was recorded during maximal voluntary contractions (MVC), and performed during shoulder abduction and wrist extension, respectively. For shoulder abduction MVC was performed in the sitting position with the shoulders 45° abducted, the elbows 90° flexed, and with the forearms pronated. For wrist extension the forearms were pronated and the wrists were in a neutral position. For both reference tests, three bilateral repetitions (four in cases when the third was the best) of maximal effort over 4 sec were performed, separated by 2 min rest periods. The muscle force was measured using strain gauge force transducers, which were placed in inflexible metal cylinders connected to metal braces positioned above the elbow for shoulder abduction and proximal to the carpal bones for wrist extension.

EMG was recorded with surface bipolar electrodes (15 × 25 mm, Ag–AgCl electrodes, type 725 01-K, Medicotest A/S, Ølstykke, Denmark), with a 20 mm interelectrode distance. The electrodes were placed bilaterally on the upper trapezius 2 cm lateral to the midpoint on the line from vertebra C7 to the acromion, and on the middle of the muscle belly of the extensor digitorum communis. The EMG signals were preamplified 1000× (bandwidth 10–3000 Hz, CMRR > 100 dB, input impedance > 5G Ω) and then amplified two times by an isolation amplifier.

2.2.3 Intramuscular blood flux: Laser-Doppler flowmetry

Microcirculation (blood flux) was recorded bilaterally from the upper trapezius using single-fiber laser-Doppler flowmetry (LDF). Local anaesthesia (0.5 ml Xylocain 10 mg/ml at each side) was applied to the skin above trapezius and Teflon catheters (Venflon 0.9 x 25 mm, BD, Helsingborg, Sweden) were inserted bilaterally by sterile technique into the upper trapezius on the middle of a line from C7 to acromion (Fig. 4). The catheter was directed caudally and laterally through the

muscle fascia of the trapezius. Hence, the insertion of the muscle fascia was some distance from the anaesthesized skin. The laser-Doppler probes (MT A500-L 120 mm, Perimed AB, Järfälla, Sweden) were inserted through the catheter, which was then withdrawn. The probes were connected to a laser-Doppler flowmeter (Periflux 4001, Perimed AB, Järfälla, Sweden) for measurements.

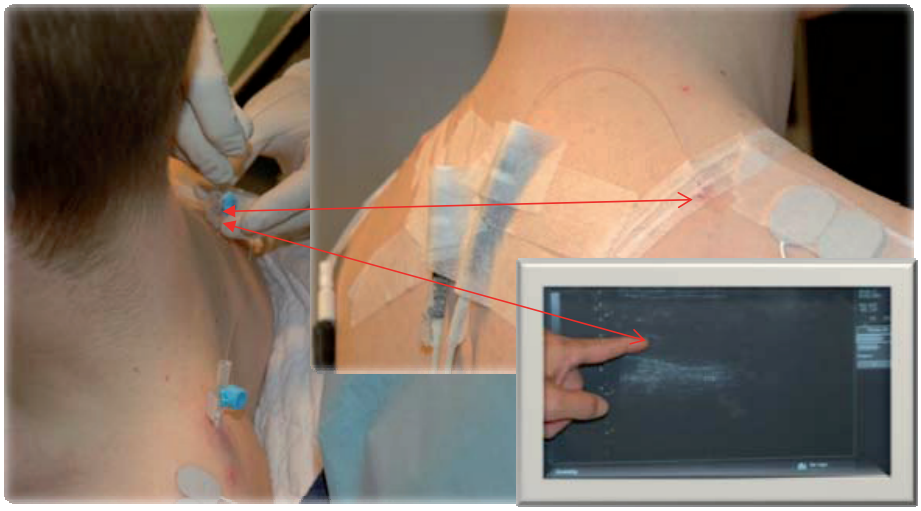

Fig. 4. Insertion and placement of probes for measurement of microcirculation. After local anesthesia, the single-fiber laser-Doppler flowmetry (LDF) probes for blood flux measurements were inserted bilaterally in upper trapezius muscles through sterile Teflon catheters (to the left). To verify the correct positions of the probes within the trapezius muscle an ultra sound scanner was used (right lower corner). The insertion positions of the LDF-probes of the upper trapezius after the withdrawal of the catheters, located on the middle of the line from C7 to acromion, and close to the surface EMG electrodes. The LDF probes were mounted to the skin with soft adhesive tape to avoid movement of the cables (to the right).

2.2.4 Blood pressure and heart rate

Mean arterial blood pressure (MAP) and heart rate (HR) were recorded continuously by the Peñaz method (Finapres, Ohmeda, USA), with a finger cuff on the third finger on the inactive hand. The MAP values were corrected for height difference between the finger and heart level (Imholz et al., 1998). The cuff was automatically deflated for 30 sec every 20 min, and the forearm and hand were covered with a blanket to be kept warm.

2.2.5 Pressure pain threshold

Pressure pain threshold (PPT) was measured with a pressure algometer with a tip size of 1 cm^2. Pressure algometry provides a reliable and valid measure of PPT (Vanderweeën et al., 1996;Kinser et al., 2009), reflecting pain sensitivity of deeper tissues (Kosek et al., 1999). The pressure was applied perpendicular to the skin at a standardized rate of 50 kiloPascals (kPa) per sec in a fixed order; right and left medial upper trapezius, right and left muscle belly of extensor carpi radialis, and sternum. The sequence was repeated three times and the mean value for each point was calculated and served as the PPT, which was defined as the pressure (kPa) when the sensation changed to a sensation of pain (Fisher, 1987). The subjects indicated the PPT by pressing a signal button attached to the algometer. It was explained thoroughly to the subject that it was the threshold and not the tolerance that was to be tested

2.2.6 Salivary cortisol

Saliva was collected with use of a sterilized cotton swab (Salivette). The subject was instructed to lightly chew the cotton swab for 30–45 sec. The saturated swab was returned to a small beaker (suspended insert) and closed with a stopper, and then placed in a freezer for later analysis.

Cortisol was measured by means of a radioimmunoassay kit (Coat-A-Count Cortisol). The samples were thawed in room temperature and centrifuged at 3000 G for 15 min. From each subject-sample two samples were derived (each of 200 µl) and analyzed, and the mean of these two samples were considered as the cortisol concentration.

2.2.7 Health complaints

A symptom questionnaire, validated by Steingrimsdottir et al. (2004;2005), rated the intensity and duration of health complaints during the preceding four weeks of the experiment. Headache; neck pain; shoulder pain; pain in the forearm, wrist, or hand; back pain; chest pain; and pain in the lower extremities were rated on

a 4-point scale for both the intensity (0 = not troubled, 1 = little troubled, 2 = quite troubled, and 3 = seriously troubled), and the duration (1 = 1–5 days, 2 = 6–10 days, 3 = 11–14 days, and 4 = 15–28 days during the last 4 weeks). The scores for intensity and duration were multiplied for each item to yield a complaint severity score, which ranged from 0 (no complaint) to 12 (severe complaint), and the mean of these scores comprised the musculoskeletal complaint severity index (MSI).

2.3 Data processing and statistical analysis

The continuous data was sampled with a frequency of 2000 Hz (LabView 7.0, National Instruments, Austin, Texas, USA). The data were re-sampled for offline analysis with a frequency of 10 Hz, and median values were then calculated over three min periods and averaged over each 15-min period.

Root mean square (rms) EMG signals were calculated over 0.1 sec periods and noise levels defined as the lowest registered rmsEMG amplitude during all registered data for each subject, were subtracted. The highest rmsEMG amplitude obtained over seven ms moving windows during MVC was used to calculate the maximal EMG amplitude (EMG_{max}). EMG values are reported as percentage of the EMG_{max} ($\%EMG_{max}$).

As the LDF method does not permit measurement of absolute values, but in arbitrary perfusion units (Leahy et al., 1999), blood flux values were normalized. The median of the three min baseline was set to 100 percent and the subsequent values are reported as percentage of baseline LDF ($\%LDF_{Baseline}$).

Statistics

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, releases 15.0 and 17.0). Independent sample *t* tests were used to explore group and sex differences and paired-sample *t* test for within-group differences. A two-tailed significance level of 5% was adopted. Spearman's rho correlation analysis was used to examine associations.

In Paper I- IV the linear mixed model analysis for repeated measurements (Fitzmaurice et al., 2004) was used to fit the best model for the time course, i.e. modeling the mean response of pain, PPT, EMG, LDF, tension, eyestrain, HR, MAP, and

salivary cortisol. Differences between genders were analyzed separately with gender included in the models. Polynomial trends (linear and quadratic trends) in time and linear spline models (piecewise linear trends) were fitted. The piecewise linear models were run with break-points (locations for the lines to be tied together) located at work task ending (i.e. at 90 min) and else at judiciously chosen time points based on visual inspection of the observed data (Fitzmaurice et al., 2004). The models were compared using a likelihood ratio test based on the maximum likelihood. Normality of the data was checked with residual plots, and due to non-normality, EMG and LDF data were logarithmically (log) transformed prior to analysis of the time course. For more details on the mixed model statistics used, see Paper I and II.

3 Main results

3.1 Paper I

Strøm V, Knardahl S, Stanghelle JK, Røe C. Pain induced by a single simulated office-work session: Time course and association with muscle blood flux and muscle activity. Eur J Pain 2008. doi:10.1016/j.ejpain.2008.11.003.

The study was undertaken to investigate if an office work model performed with time pressure and precision demand elicited responses in healthy and pain-free subjects.

The main results were that pain increased considerably during the office work, steeper after the initial 45 min of the work task, and reaching peak pain at the work-end (i.e. at 90 min), 43 $\pm$ 28 and 32 $\pm$ 27 mm for active and inactive shoulder and neck, respectively (Fig. 5a). After 30 min recovery the pain was still significantly higher than the baseline values ($p < 0.01$). General tension and eyestrain also increased, but exhibited different time course than that of the pain; i.e. steep initial increase and then leveling off.

The muscle activity in the upper trapezius increased during the work, similar in both the active and passive side, reaching peak levels close to 3 % of EMG_{max}. After cessation of the work task, an immediate reduction to baseline levels was seen in the muscle activity of both sides of trapezius.

The blood flux in the active trapezius increased to 167 $\pm$ 82 % of the baseline level ($p = 0.002$) at the onset of work and to 126 $\pm$ 46 % ($p = 0.008$) in the inactive trapezius. The blood flux of the active side was elevated for 30 min followed by a falling trend. In the inactive trapezius there was an initial short-lasting blood flux increase. At cessation of the work the blood flux fell back to the baseline levels in both sides (Fig. 5b).

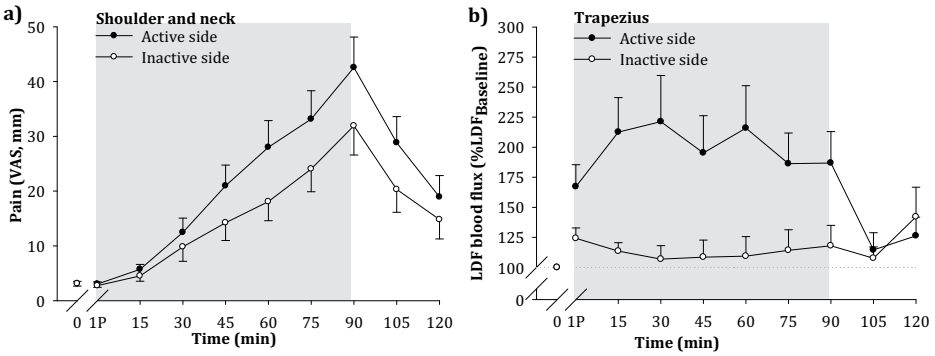

Fig. 5. Pain and blood flux. Mean values of ratings at visual analogue scale (VAS; mm) for a) pain in the active and inactive shoulder and neck, and b) laser-Doppler flowmetry (LDF; % of baseline LDF) in the active and inactive upper trapezius, at baseline (0), after completion of the first page of the work-task (1P) and after each 15 min period of the 90 min computer work task and 30 min recovery. The ticks represent + 1 standard error of the mean and the shaded area the working period.

No significant interactions were found between time and muscle activity in relation to pain. In contrast, there were significant interaction terms between time and blood flux on pain for both the active and inactive sides, indicating that the association between pain and blood flux develops over time. After 45 and 30 min in the active and inactive side, respectively, the blood fluxes tended to exhibit negative correlations with pain.

3.2 Paper II

Strøm V, Røe C, Knardahl S. Work-induced pain, trapezius blood flux, and muscle activity in workers with chronic shoulder and neck pain. Pain 2009;144:147-155.

In the pain group the time course of pain that was similar in both the active and inactive shoulder and neck exhibited a significant quadratic time effect, i.e. a pronounced increase in the pain intensity during the *first* part of the work task (Fig. 6). This differed from the non-constant increase in pain exhibited during the *last* part of the work task found in the reference group (Fig. 6).

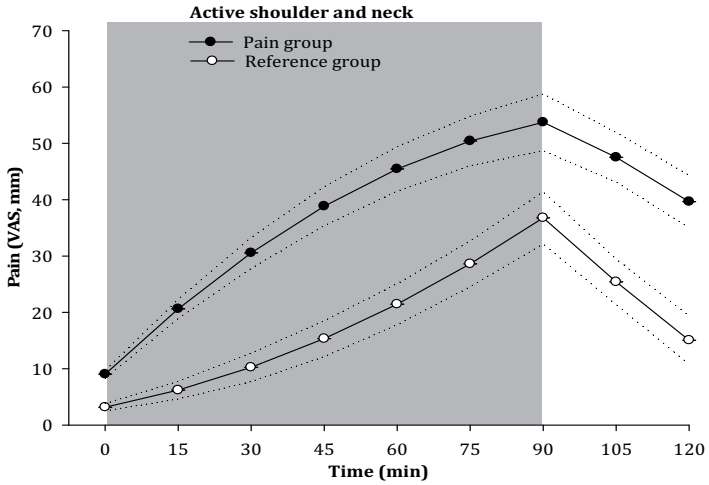

Fig. 6. Time course model of the pain ratings. Illustration of the best fitted models of the pain intensity ratings (at visual analogue scale (VAS; mm) of the active shoulder and neck in subjects of the pain (n = 22) and reference groups (n= 26) to the 90 min office work task (shaded area) and the 30 min recovery period. The non-linear response significantly differed between the groups. Dotted lines indicate 95% confidence interval.

The women with chronic pain exhibited a greater increase in pain (on average 15 mm per time unit, $p < 0.001$) than did men and in a quadratic fashion ($p = 0.01$). As in the reference group, the shoulder and neck pain of subjects in the pain group peaked at 90 min (68 ± 18 mm versus 44 ± 26 mm, $p = 0.02$, in women and men, respectively). After 30 min of recovery, the pain intensity of the pain group was still higher than at baseline in both sides of the shoulder and neck ($p < 0.001$), and higher than in the reference group ($p < 0.01$).

Starting the work task increased the blood flux in the active upper trapezius of the subjects in the pain group to 226 ± 168 $\%LDF_{Baseline}$, $p = 0.001$), and to 128 ± 35 $\%LDF_{Baseline}$ ($p = 0.004$) in the inactive trapezius. The initial blood flux increase in the active side was greater in the pain-afflicted men than in the pain-afflicted women (285 ± 230$\%LDF_{Baseline}$ vs. 183 ± 92$\%LDF_{Baseline}$, $p = 0.04$). The blood flux peaked at 15 min in the active side and at 45 min in the inactive side. During the first 15 min of the recovery, the blood flux values of the subjects in the pain group were still significantly elevated above baseline values in both sides of the trapezius ($p < 0.05$), and significantly higher than that in the reference group ($p < 0.05$).

The EMG levels during the office work were low (>4% EMG_{max}), and similar in the pain and reference groups. No significant correlations were found between muscle activity and pain in either group.

Significant correlations between pain and blood flux appeared towards the end of the work task. In the pain group higher blood flux values correlated with higher pain, whereas in the reference group, lower blood flux correlated with higher pain (Fig. 7).

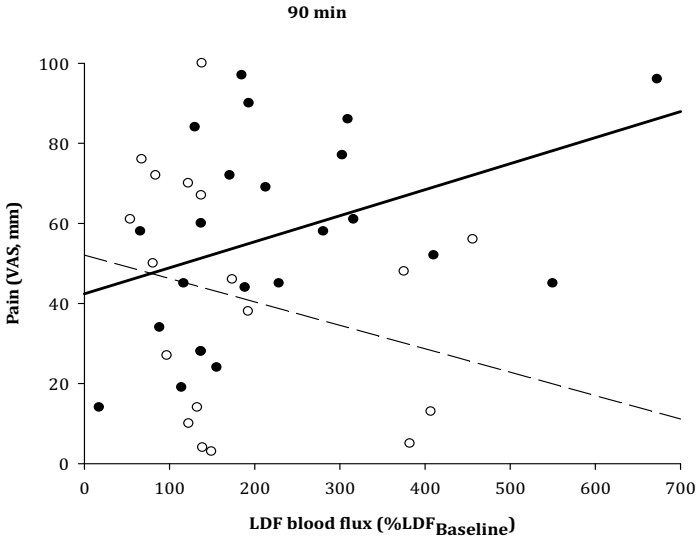

Fig. 7. Pain in relation to blood flux. Scatter plots with regression lines of pain ratings on visual analogue scale (VAS; mm) in the active shoulder and neck in relation to the corresponding upper trapezius laser-Doppler flowmetry (LDF; % of baseline LDF) blood flux in subjects with chronic shoulder and neck pain (n = 22) and healthy pain-free reference subjects (n = 26), at 90 min of the office-work task.

3.3 Paper III

Strøm V, Røe C, Matre D, Knardahl S. Pain induced by simulated office work: Pressure pain thresholds, salivary cortisol, and performance in subjects with chronic shoulder and neck pain and in healthy pain-free subjects. Submitted

The main findings in this paper were that PPT's of the active (Table 1) and inactive trapezius muscles were significantly reduced in both groups after 15 min and 30 min of the recovery period compared with the pre work levels. For the active extensor carpi radialis the PPT reached statistically significant reductions after 30 min. For the inactive extensor carpi radialis and sternum the PPT tended to be lowered in the pain group after 15 min recovery. There were no significant differences between the groups in any of the measure sites. Negative correlations were found in both groups between the pain intensity ratings at the end of the work task and the PPT's after the task.

Table 1. Estimated regression coefficients and standard errors (SE) based on the fitted linear models[a] for the pressure pain threshold (PPT, kPa) data of the active side of the upper trapezius muscle in subjects of the pain and reference groups in response to a 90 min simulated office work.

		Estimate of the			
Active upper trapezius	Time	β	SE	*t*	*p*-value
Pain group					
(β1) Intercept		343	34	10,1	< 0.001
(β2) $Time_{post15}$	15 min post	-32	14	-2,2	0.032
(β3) $Time_{post30}$	30 min post	-23	10	-2,3	0.030
Reference group					
(β1) Intercept		358	31	11,4	< 0.001
(β2) $Time_{post15}$	15 min post	-30	9	-3,2	0.004
(β3) $Time_{post30}$	30 min post	-32	11	-3,1	0.005

[a]Linear mixed models for repeated measurements fitted with unstructured or first-order autoregressive covariance structure.
(β1) = Estimates of the pre work task PPT value.
(β2) = Estimates of the change in PPT from the pre work task to 15 min post work task.
(β3) = Estimates of the change in the PPT from the pre work task to 30 min post work task.

For subjects in both groups the salivary cortisol concentration fell significantly in the period from startup to the baseline measures (2.4 $\pm$ 4.1 nmol/l decrement, p = 0.007, in the pain group, and 4.1 $\pm$ 3.0 nmol/l decrement, $p < 0.001$, in the reference group), with no difference between the groups ($p = 0.4$). The time course analysis of the salivary cortisol levels, starting from baseline and through the 90 min work task and 30 min recovery, showed no significant changes in either group.

3.4 Paper IV

Strøm V, Røe C, Knardahl S. Coffee intake may attenuate development of pain during office work. Submitted

Since 20 (38%) of the subjects had consumed coffee (on average 1 h 18 min before start) this paper sought to determine if the coffee consumers exhibited different time course in the pain development and blood flux than the non-coffee consumers.

During the work task the coffee consumers exhibited significantly lower pain increase than those who had abstained from coffee ($p < 0.01$; Fig. 8). Both the coffee consumers and abstainers exhibited elevated blood flux levels in the trapezius throughout the work task, but there were no significant differences between coffee drinkers and coffee abstainers in the time course of blood flux.

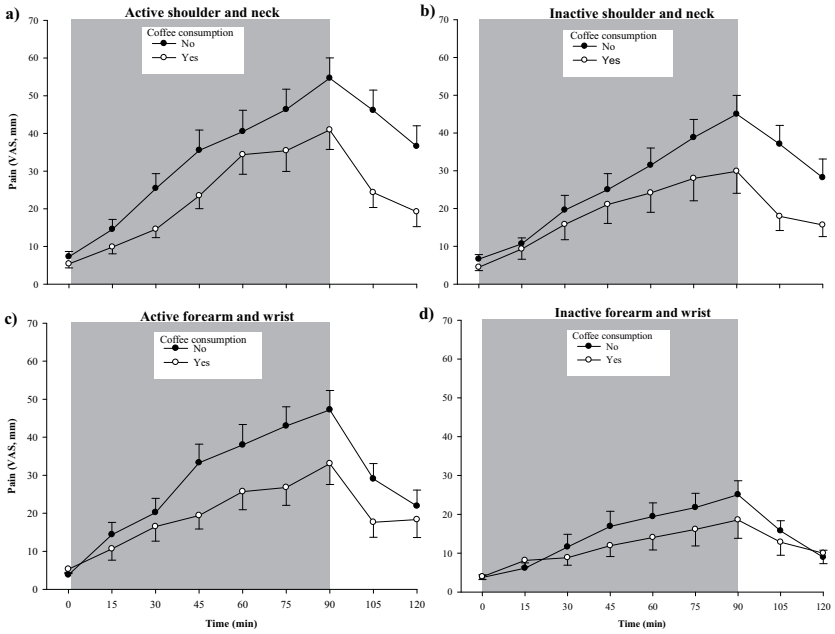

Fig.8. Mean pain intensity in (a) the active shoulder and neck, (b) inactive shoulder and neck, (c) active forearm and wrist, and (d) inactive forearm wrist, rated on a visual analogue scale (VAS; mm) at baseline (0), and every 15 min throughout the 90 min office-work task and 30 min recovery, in subjects that had consumed one cup of coffee before start (n = 20, open circles), and in subjects that had abstained from coffee consumption (n = 32, filled circles). The ticks represent + 1 standard error of the mean and the shaded area the 90 min work task period.

4 Discussion

4.1 Methodological aspects

4.1.1 Study sample

An essential methodological concern in experimental research is to what extent the study sample is representative of a larger population. The present study sample was recruited via the Internet and local papers and comprised fulltime working subjects representing a variety of occupations (>40 different professional titles). The participants had a higher education level than that in the general Norwegian population; Seventy nine percent of the subjects had more than 13 years of education compared with 26% in the general Norwegian population (Norwegian Statistics, 2006). The education level was, however, similar in both the pain and reference groups.

The main criteria for being included in the pain group was the presence of pain in the shoulders or neck for at least 2–3 days per week during the previous 4 weeks and tender points in corresponding muscles. A clinical examination was performed by a specialist in physical medicine and rehabilitation and verified that all subjects had tender points in the upper trapezius muscles and that none fulfilled the ACR criteria for fibromyalgia (Wolfe et al., 1990). All subjects reported shoulder and neck pain for more than 4 weeks, ranging from 6 months to more than 10 years, thus they met customary criteria for chronicity. In addition the reporting of health complaints during the 4 weeks before the study indicated that they were more prone to musculoskeletal health complaints, however, not severely affected. The latter is consistent with the findings of Steingrimsdottir et al. (2004) who reported low-level health complaints in a working population monitored for 30 months. The pain group thus comprised well-educated fulltime working subjects with longstanding, but probably not severe shoulder and neck pain.

4.1.2 Design and methods

Previous studies of simulated real-life computer work have used the Stroop Color Word Test (CWT) (Lundberg et al., 1994;Larsson et al., 1995) or a complex two

choice reaction-time task (Wærsted et al. 1991;1994;Wærsted and Westgaard, 1996;Nilsen et al., 2006;2007). Results from these computer work tasks are not easily transferred to real work situations using a computer mouse (Wahlström et al., 2002). Others have used the computer mouse during specially designed tracking tasks at different precision levels (Laursen et al., 2001;Røe and Knardahl, 2002;Visser et al., 2004). The present study was conducted in a laboratory setting and designed to simulate realistic office work performing word processing, which is a feature of computer office work (Punnett and Bergqvist, 1997); using the computer mouse to mark, copy, paste, and delete continuously for 90 min with high hand precision demands and time pressure. The work task model sought to resemble real life office work in order to enhance the external validity. It seems that the model used succeeded both in inducing pain and pressure hyperalgesia, and in producing physiological alterations during the work session. The change in the salivary cortisol levels seen in response to the work task for subjects in both groups was small compared to laboratory studies of speech and mental arithmetic's in front of an audience (Schommer et al., 2003), indicating that the imposed work task in the present study induced a modest arousal in the participants.

The muscle-activity levels in the upper trapezius during the work task in the present study were very low and slightly lower than in other studies with simulated light work (Røe and Knardahl, 2002;Visser et al., 2004;Rosendal et al., 2004a). The present EMG data both from the shoulders and forearms are in accordance with values reported from workplace measurements of computer work (Jensen et al., 1998;Visser et al., 2004; Crenshaw et al., 2006).

The work task posed a high demand for hand precision since all errors to be corrected necessitated marking of small sized letters in the text. A pilot study comparing correction of a standardized text with errors in the letter "i" versus the letter "m" revealed that correcting the "i" errors was significantly more time consuming, thus indicating a higher demand of precision.

Time pressure was in the present studies induced by an individual performance target based on the pretest performance. Attaining the target elicited a monetary reward. Receiving a money reward has been reported to affect performance during a computer work task (Wærsted et al., 1994). Subjects in the pain group completed fewer pages than the subjects in the reference group, i.e. they

exhibited a slower work-pace, and hence a lower production. Motivation and engagement in the work task might have affected the performance differently in the groups. However, the performance relative to the individual target and the obtained reward were not different between the groups in the present study, and epidemiological studies have found self reported productivity to be reduced when pain is present (Hagberg et al., 2002;van den Heuvel et al., 2007).

Moreover, it seems that the duration of the imposed office work task have made significant contribution to the results at hand. For the healthy pain-free subjects a critical time point appeared to have occurred at about 30-45 min of the work where the pain started to increase in an exponentially manner (Paper I). It thus seems that tasks shorter than 30 min may not capture significant pain development in pain-free subjects during continuous office work with time pressure and precision demands. Previous studies of low-load exercise and simulated office work that have measured the trapezius microcirculation with the LDF method have only recorded short exercise periods (< 3 min) (Larsson et al., 1993a;1993b;1994;Røe and Knardahl, 2002). The time course of the blood flux in the active trapezius throughout the office-work task exhibited increased levels during the initial periods and decreased toward the end of the work task (similar in both groups). The blood flux correlated positively with the muscle activity for the first 15 min in the pain group and for the first 30 min in the reference group, possibly reflecting muscle fiber recruitment and local metabolic needs (Thomas and Segal, 2004) or the influence of central command. However, no such relationship was seen after these times, pointing to other regulatory mechanisms. The time course of the blood flux in the inactive side of the upper trapezius muscle was dissimilar in the groups; in the pain group the blood flux increased modestly for 45 min and remained elevated thereafter, while in the reference group the blood flux approached the baseline level after the initial periods.

The time-control test indicated that performing the office work without work demands elicited different responses both in terms of pain, tension, blood flux, and muscle activity. The imposed work demands in the present office work model, i.e. the high precision demand, the time pressure, and the duration of the task, thus seemed to have made significant influence of the present results. It remains to elucidate the individual effects of these demands.

Statistical consideration

Linear mixed model analysis for repeated measurements (Fitzmaurice et al., 2004) was used in all included Papers to fit the best model for the time course. More commonly used is the repeated-measures design of analysis of variance (ANOVA; Altman, 1996). ANOVA yields correct tests only under conditions of sphericity, i.e. under the assumption that for any pair of repeated measurements, the variance of the difference between them is constant and the differences between any two pairs of measurements are not correlated (Bagiella et al., 2000). Measures on the same subject close in time tend, however, to be more highly correlated than measures far apart in time, and variances of repeated measures often change with time (Littell et al., 1998). Thus, the probability of falsely rejecting the null hypothesis is higher than the selected significance level when sphericity does not hold (Bagiella et al., 2000). Mixed models are an alternative procedure for the analysis of repeated-measures data, and these models also handle missing data more effectively (do not cause all data to be ignored), and are more flexible (Bagiella et al., 2000).

4.1.3 Pain measurements

Pain was rated on a visual analogue scale (VAS), which has been reported to be a valid instrument both for healthy subjects and for patients (Price et al., 2008), and high repeatability has been demonstrated (Rosier et al., 2002). One may speculate if expectancy contributed to the pain increase since the participants knew in advance that the purpose of the study was to investigate how the imposed office work influenced pain development. However, they were not allowed to see previous ratings during the task, and it seems unlikely to remember the exact position of previous ratings.

The results from the control session (see Fig. 2a) indicated a minor increase in the pain intensity when the task was performed without any demands. Thus, sitting still trying not to move for so long time *per se* may be painful, and might thus contribute to the pain increase seen during the experimental session. Furthermore, the intramuscular LDF-probes bilaterally in the upper trapezius might have caused pain. However, a pilot study of the complete experimental session, but without

insertion of LDF probes, revealed a time course of pain (data not shown) similar to that presented in Paper I. Moreover, four of the subjects (two in each group) reported that pain in the shoulders was a consequence of the laser-Doppler probes insertion. Their data were excluded from the analysis of pain.

4.1.4 Measurements of microcirculation

The LDF method, based on Doppler-shift in wavelength of infrared light, was first introduced by Stern (1975) and later applied *in vivo* by Salerud and Öberg (1987). This method makes continuous real-time assessment of the microvascular blood perfusion in muscle possible (Salerud and Öberg, 1987). The LDF method has produced valid results during varying levels of static contractions in the upper trapezius (Larsson et al., 1993a;1993b;1996) and the reliability has been reported for trapezius muscle blood flux (Røe et al., 2008).

A limitation of this method is that LDF does not give an absolute measure of blood perfusion (Leahy et al., 1999), but merely arbitrary units. Therefore, the present blood flux values were normalized. The median of the three minutes baseline was set to 100 percent and the subsequent values were reported as percentage of this value.

The LDF technique is very sensitive to movements of the probes (Jensen et al., 1995b), thus one challenge with this method is to avoid artifacts. In the present study measures were taken to avoid unintended movement in that the probes and cables were taped to the skin with soft adhesive tape and the subjects were instructed not to move unnecessary. In order to check if movement of the head during the work task influenced on the LDF results a specialized gear was mounted on the subjects head for continuous recording of head movements. These data remains to be analyzed, however, the blood flux exhibited different time course for the active and inactive side concomitant to surface EMG levels similar in both sides. During the whole work task session the subjects were observed by the investigator and any major movement seen was recorded for later use in the data analysis (rejection of movement artifacts). Most artifacts were however readily seen at visual inspection of the LDF recordings and these data were excluded. Hence, movement artifacts should not affect the present data in a systematic way.

The insertion of the LDF probe may cause hyperaemia by tissue trauma (Staxrud et al., 1991). We can not rule out the presence of trauma in the trapezius. However, occurrence of rhythmic variations in the LDF signals with a frequency of 4-10 cycles/min was verified, which is taken as a sign that the introduction of the probes into the muscle tissue not seriously has traumatized the tissue volume under study (Øberg, 1990). Also, the thin fibers used with diameter of 0.5 mm should minimize the tissue trauma (Kvernebo et al., 1990).

A relatively large between-subject variation was seen in the LFD measurements. Large variability could be due to local variation of muscle blood flow (Larsson et al. 1993a). Since the measurement volume from a LDF probe is in the area of one cubic millimetre it is sensitive to spatial heterogeneity (Larsson et al., 1994, Staxrud et al., 1996). That is, if the probe is positioned close to an area with only capillary vessels the LDF signal is normally much less than when the probe is positioned closed to an artery (Leahy et al., 1999). Furthermore, the values from such small volumes my not be representative for the muscle as a whole.

The correct position of the probes within the trapezius muscle was at the time of insertion verified by use of an ultra sound scanner. The position was however not verified later on during the work task, thus a possibility exist that displacements of the probes within the muscle might have occurred (Staxrud et al., 1996), and have likely occurred in the one subject that increased the flux values considerably after a major arm movement (Paper I).

The increased microcirculation in the active trapezius seen in the present study seems comparable to similar findings during low-level static shoulder and neck exercise with other measurement techniques. With a microdialysis method, where blood flow is estimated from the outflow-to-inflow ratio of a tracer (ethanol or $^{3}H_2O$) in the dialysate (Hickner et al., 1994;Stallknecht et al., 1999), increased trapezius muscle blood flow in response to 30 min static shoulder exercise at 10 % MVC (Ashina et al., 2002), or to 20 min low-level exercise of moving small pegs (Rosendal et al., 2004b;Gerdle et al., 2008a;b) have been reported. Near-infrared spectroscopy (NIRS), a non-invasive method widely used for measuring tissue oxygenation (Boushel and Piantadosi, 2000), may be used for blood flow measurements with venous occlusion (van Beekvelt et al., 2001). Thus, NIRS seems unsuitable for trapezius blood flow measurements.

4.1.5 Measurements of muscle activity

EMG values were reported as percentage of the maximal EMG obtained during MVC (Hägg et al., 2000). Pain may influence the MVC measures (Graven-Nielsen et al., 1997). Other studies have shown no influence of shoulder muscle pain on MVC (Røe et al., 2000). In the present study there were no significant differences between the groups in MVC of either side of the shoulders. Thus, the EMG_{max} results should provide reliable EMG levels.

The relative static load on the shoulders ($\%EMG_{max}$) was very low throughout the work task in both groups. The upper trapezius EMG reached a peak level at about 3-4 $\%EMG_{max}$, somewhat lower than in other studies with simulated light work (Røe and Knardahl, 2002; Visser et al., 2004; Rosendal et al., 2004a). The time course of EMG in the inactive trapezius was similar to that of the active side. The inactive forearm was resting at the table without movement throughout the work-task. One may speculate whether the EMG increase seen during the last part of the work is due to muscle fatigue. However, the muscle activation level during the work was low and fatigue development during contractions at such low activation levels is minimal (Sjøgaard et al., 1986). Eye strain may contribute to increased static load in the shoulder muscles (Hagberg and Sundelin, 1986), and trapezius muscles stabilize the head to ensure a stable visual field (Dutia, 1991).

4.2 Discussion of main findings

4.2.1 Pain

A striking finding of the present thesis is the substantial increase in pain intensity during the work task in both groups. This seems to demonstrate that one single session of office work may produce considerable pain even in healthy pain-free subjects. In the chronic pain subjects the pain intensity in the shoulder and neck rose already from the onset of the work, while in the reference group the pain began to increase in an exponentially manner after 30-45 min of the work. The substantial pain increase for the reference subjects seems to contrast with previous studies of other tasks, reporting peak pain intensity lower than 10 mm on the VAS in the

shoulders and neck among healthy pain-free subjects (Bansevicius et al., 1999; Rosendal et al., 2004a; 2005; Nilsen et al., 2006). A repetitive low-force exercise (moving short wooden sticks) for 20 min produced pain intensity in female patients with chronic trapezius myalgia (Rosendal et al., 2004b; 2005), that was similar to the present results of the chronic pain females. A common finding in all the above mention studies is increasing trends in pain intensity across exercise time.

Both the pain-afflicted subjects and those in the reference group exhibited similar pain responses in the active and inactive sides of the shoulder and neck. It seems surprising that the inactive, and relaxing, side of the shoulders should be so painful. It is possible that it is difficult for subjects to distinguish pain from the two sides of the shoulders and neck. The pressure pain thresholds were however reduced after the work task both in the active and inactive side of the trapezius (Paper III), and the PPT's after the task were negatively correlated with the perceived pain intensity.

We also found similar pressure pain thresholds in all measurement sites in both the pain and reference groups. This finding contradicts several studies reporting lower PPT in patients with chronic shoulder and neck pain compared to healthy controls (Takala 1990;Levoska 1993;Hägg and Äström, 1997;Rosendal et al., 2004). The chronic pain subjects included in the present study were fulltime workers and thus perhaps less pain afflicted than those included in the above mention studies.

Even after 30 min of rest some pain remained in the subjects of both groups, but significantly more in the pain group. There was a reduction in PPT from pre- to post work task that was similar in both groups. A decrease in mechanical pain threshold is associated with sensitization of muscle nociceptors (Mense, 2003). Peripheral pathologic changes (e.g. injury, inflammation, and changes in muscle blood flow) causing peripheral sensitization of nociceptors have been suggested as possible participating factors to increased pain sensitivity (Mense, 2003). Recent studies have found evidence for an altered chemical environment in the trapezius muscle of pain-afflicted subjects, including increased levels of serotonin, glutamate, bradykinin, kallidin, interleukins, lactate, and potassium (Ashina et al., 2002;Rosendal et al., 2004;2005;Gerdle et al., 2008a;2008b;Shah et al., 2008), molecules that may affect nociceptors and contribute to the sensitization of spinal dorsal horn neurons (Mense, 2009).

A significant finding was that the women with chronic pain exhibited a more pronounced pain response than the men (Paper II and III), whose pain response resembled that of the reference group. These results are consistent with several recent studies showing sex differences in experimental muscle pain in the trapezius (Ge et al., 2005a;2005b; Falla et al, 2008). A higher prevalence of musculoskeletal pain in the upper extremities is reported in women compared with men (Bergenudd et al., 1988;Wijnhoven et al., 2006), and women also seem to report more pain when working with computers (Ekman et al., 2000;Jensen, 2003;Juul-Kristensen et al., 2004; Andersen et al., 2008). In addition, the response to the health complaints questionnaire indicated that those having headache in addition to the chronic shoulder and neck pain responded to the work task with stronger pain. The chronic pain women reported more severe headache than the men.

We found a possible effect of coffee on pain (Paper IV). However, since a controlled randomized design of the coffee consumption not was used a lot of uncertainties about the association between coffee intake and differences in pain-perception during the office work task exist. The quantity of coffee consumed was self-reported. One cup was the maximal allowed limit, but the size of a cup and the caffeine dose may vary. The time from coffee intake to start of the experiment was not standardized. The mean time spent from coffee consumption until start was, however, within the half-life of caffeine (Fredholm et al., 1999). Nevertheless, the attenuated pain response seen for the coffee drinkers was significant for all measured pain sites even when adjusted for sex and the presence of chronic pain, thus, a possible effect of coffee consumption cannot be excluded in the present study. Other studies have reported attenuated muscle pain after caffeine administration during dynamic exercise of >60% of maximal capacity (Motl et al., 2003;O'Connor et al., 2004), and during ischemic (Myers et al., 1997) and eccentric muscle contractions (Maridakis et al., 2006). The caffeine doses in these studies (>5 mg/kg) were probably higher than those assumed in the present study. The possible mechanism of caffeine on the pain response in the present study is uncertain. Caffeine has high affinity to both adenosine A_1 and A_{2A} receptors (Fredholm, 1999). Adenosine may exert its influence on pain via peripheral C-fiber involvement and within the central nervous system (Sawynok and Liu, 2003). Activation of A_1 receptors inhibits

nociception both in the periphery and at the spinal level, while activation of A_{2A} receptors augments pain peripherally, but seems to have no direct effect on nociception at the spinal level (Sawynok and Liu, 2003). Thus, the action of caffeine depends on the type of receptors that is blocked and on tissue in which the receptors are located.

4.2.2 Pain in relation to the microcirculation and muscle activity

The findings reported in Papers I and II indicated that there was local vasodilation in the trapezius throughout the office work in both groups. This suggests that the regulation of the microcirculation during very low level of muscle activity is unaltered in subjects with chronic shoulder and neck pain. Several studies of low-level work-load of the shoulders have reported elevated local muscle blood flow, in both healthy controls and patients with pain in the shoulders, neck or head (Ashina et al., 2002; Rosendal et al., 2004b; Gerdle et al., 2008), concomitant to increased levels of interstitial lactate concentrations (Ashina et al., 2002; Gerdle et al., 2008). Other studies indicate that subjects with chronic pain conditions exhibit disturbed local muscle blood flow (Larsson et al., 1994;Larsson et al., 1998;1999;Ashina et al., 2002). However, a common finding in all these studies was that the blood flow levels in the upper trapezius were elevated above resting levels. The limited ability to increase blood flow in subjects with pain reported by Larsson et al. (1994;1998;1999), occurred only "above a certain level" during stepwise-increased static contractions, a level probably higher than that during office work with a computer. There was no significant change in the local muscle oxygen saturation in the trapezius, in 30 and 60 min of low-load work, despite increased intramuscular concentrations of lactate and glutamate (Flodgren et al., 2006). It seems that during contraction levels below ten percent of MVC the blood flow is sufficient to maintain the energy supply (Sjogaard et al., 1988). Therefore, the computer work in the present study should not compromise circulation or produce energy crisis.

Significant associations were found between pain and blood flux in both groups, however in opposite directions; in the pain group those with the highest blood flux values reported the highest pain level, while in the reference group those subjects exhibiting lower trapezius muscle blood flux reported the strongest shoulder and

neck pain. It is difficult to find an adequate explanation for these findings, however, it might indicate that different mechanisms are involved in the pain development among the groups, and that blood flow *per se* (vasodilation) might not be a pivotal factor generating shoulder and neck pain during office work. Moreover, for subjects with chronic pain the finding may support the hypothesis that the blood vessel–nociceptor interaction is important to the activation of muscle nociceptors (Knardahl, 2002;2005).

The significant interactions between the pain in the shoulders and neck and the trapezius muscle blood flux developed with the work time in both groups. The blood flux increased from the start of the work task, and the change from the increasing to decreasing trend corresponded in time with the increase in pain in both groups. While pain increased substantially after 30 min of the work-task for subjects in the reference group, blood flux in the active trapezius started a falling trend, and a negative correlation was found after 45 min of work. There may be an unknown time-lag between local peripheral intramuscular mechanisms and the development of pain in healthy subjects, hence, the correlations between blood flux and pain measurements may not reveal pathogenetic relations. Furthermore, it was not possible in the present study to elucidate the direction of this relationship, i.e. if the flux causes the pain or vice versa.

The blood flux did not return to the baseline level on either side during the initial 15 min of the recovery in the pain group, as opposed to an immediate return to the baseline level in the reference group. Rosendal et al. (2004) reported increased trapezius blood flow after a 20 min low-force exercise in subjects with TM, but not in healthy controls, and elevated intramuscular lactate levels during rest and exercise in the TM group. There was no post-exercise hyperaemia in the present study, indicating that energy deficit did not play a role. A low-level static contraction increased algogenic vasodilating kinins which correlated with pain in the trapezius (Boix et al., 2005). Injury, inflammation or changes in muscle blood flow are factors that may contribute to peripheral sensitization of nociceptors (Mense, 2003). We found the PPT bilaterally in the trapezius to be significantly reduced 15 min and 30 min after the task. However, the reductions in PPT were similar in both groups.

No significant correlations were found between the reported pain levels and the observed muscle activity levels in either group or time point. This lack of an

association between pain development and muscle activity are in support of recent studies reporting that the trapezius muscle activity does not account for the pain in the shoulders and neck (Westgaard et al., 2001;Mork and Westgaard, 2006; Nilsen et al., 2006), but contrasts earlier studies suggesting a relationship between muscle activity and pain (for review see e.g. Visser and Dieën, 2006).

5 Conclusions

1. Office work involving time pressure and precise hand movements induced substantial pain both in people with chronic pain and in healthy pain-free subjects.
2. The trapezius muscle activity increased during the pain provoking office work, but remained at a very low level (<4% EMGmax).
3. Office work induced trapezius vasodilation, but the blood flux did not return to resting values during recovery in subjects with chronic shoulder and neck pain.
4. Simulated office work with time pressure and hand precision demands for 90 min induced deep tissue hyperalgesia in shoulder muscles both in subjects with and without chronic shoulder and neck pain.
5. People with chronic shoulder and neck pain exhibited different time course in the pain response than the healthy pain free subjects during the office work, despite similar time course of both the trapezius muscle activity and microcirculation, and the pressure pain thresholds.
6. The pain development was not associated with the trapezius muscle activity in either group or at either time during the office work.
7. The pain development was associated with trapezius vasodilation in both groups and the relationship became stronger with time spent on the work.
8. Subjects who had consumed one cup of coffee before starting a pain provoking office work task exhibited attenuated pain development compared with the subjects who had abstained from coffee intake, but without differences in intramuscular blood flux.

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I

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II

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Strøm V, Røe C, Matre D, Knardahl S. Pressure pain thresholds and salivary cortisol in response to simulated office work in subjects with and without chronic shoulder and neck pain. Submitted.

III

This article is removed.

Strøm V, Røe C, Knardahl S. Coffee intake and development of pain during office work. Submitted.

IV

This article is removed.

ERRATA

The following changes have been made in the text since submission to the doctoral committee:

Page II (Contents) "2.1. Subjects" is changed to "Subjects"

Page 11 (subheading) "**2.1. Subjects**" is changed to "*Subjects*"

Page 13 (line 6 below the figure text) "… as described under the paragraph 2.1 (see above)" is changed to "… as described above".

Page 15 (line 2) "On the experimental day …" is changed to "At the experimental day …"

Page 15 (lines 15-16) "… to the computer screen with the arms resting at the computer table to ensure comfortable seating …" is changed to "…to the computer screen to ensure comfortable seating, with the arms resting at the computer table …"

Page 17 (line 11) "… at the pretest the pain group …" is changed to "… at the pretest the subjects of the pain group …"

Page 18 (line 11) "4 s" is changed to "4 sec"

Page 25 (4th line from the bottom) "for woman and …" is changed to "in women and … "